Platform trial

A platform trial, also known as an umbrella trial or master protocol trial, is a type of clinical trial design used in medical research to evaluate multiple treatments simultaneously within the same trial infrastructure. This approach allows for more efficient and flexible testing of various treatments for a particular disease or condition.

In a platform trial, participants are often randomized to different treatment arms, each receiving a different investigational treatment or standard of care. New treatments can be added or removed from the trial over time based on emerging evidence, allowing for adaptive trial designs.

Key features of platform trials include:

Efficiency: Platform trials can evaluate multiple treatments concurrently, reducing the time and resources required to assess each treatment separately.

Flexibility: The trial design allows for adaptive modifications based on accumulating data, such as dropping ineffective treatments or adding promising ones.

Statistical Power: By pooling data across treatment arms, platform trials can enhance statistical power, enabling more reliable conclusions about treatment efficacy.

Comparative Effectiveness: Platform trials facilitate direct comparisons between different treatments, aiding in the selection of the most effective therapies.

Innovation: These trials encourage innovation by providing a framework for testing new treatments and combinations of therapies.

Platform trials have been increasingly used in various fields, including oncology, infectious diseases, and rare diseases, to expedite the development of new therapies and improve patient outcomes. Examples of platform trials include the REMAP-CAP trial for severe pneumonia and the I-SPY 2 trial for breast cancer.

Performing a platform trial involves careful planning, execution, and analysis. Here are the general steps involved in conducting a platform trial:

Define Research Question and Objectives: Clearly define the research question, objectives, and hypotheses of the trial. Determine the disease or condition of interest, the treatments to be evaluated, and the primary endpoints to assess treatment efficacy.

Design the Trial Protocol: Develop a detailed trial protocol outlining the study design, eligibility criteria, treatment arms, randomization procedures, outcome measures, statistical analysis plan, and operational procedures. Consider incorporating adaptive design elements to allow for modifications based on accumulating data.

Obtain Regulatory and Ethical Approvals: Obtain approval from relevant regulatory authorities (e.g., FDA, EMA) and ethics committees or institutional review boards (IRBs) before initiating the trial. Ensure compliance with applicable regulations, guidelines, and ethical standards.

Establish Trial Infrastructure: Establish the necessary infrastructure, including clinical trial sites, data management systems, monitoring procedures, and safety monitoring committees. Implement standardized procedures for participant recruitment, informed consent, data collection, and adverse event reporting.

Recruit and Randomize Participants: Recruit eligible participants according to the predefined inclusion and exclusion criteria. Randomize participants to different treatment arms using appropriate randomization techniques (e.g., block randomization, stratified randomization) to ensure balance across treatment groups.

Administer Treatments and Monitor Participants: Administer the assigned treatments to participants according to the trial protocol. Implement procedures for treatment monitoring, dose adjustments, and adherence monitoring. Monitor participant safety and assess treatment-related adverse events throughout the trial.

Collect and Manage Data: Collect relevant data on participant demographics, medical history, treatment responses, and outcomes according to the predefined data collection plan. Utilize electronic data capture systems or other data management tools to ensure accurate and secure data collection and storage.

Implement Adaptive Design: Implement adaptive design elements, such as interim analyses, treatment modifications, and sample size re-estimation, as specified in the trial protocol. Monitor accumulating data to make informed decisions regarding treatment continuation, modification, or termination.

Conduct Statistical Analysis: Analyze the trial data using appropriate statistical methods to assess treatment efficacy, safety, and comparative effectiveness. Evaluate primary and secondary endpoints based on predefined analysis plans. Consider adjusting for multiplicity and controlling type I error rates in the analysis.

Interpret Results and Disseminate Findings: Interpret the trial results in the context of the predefined research objectives and hypotheses. Prepare comprehensive study reports and manuscripts for publication in peer-reviewed journals. Present findings at scientific conferences and disseminate results to relevant stakeholders, including clinicians, researchers, patients, and regulatory agencies.

Follow-up and Long-term Monitoring: Conduct long-term follow-up assessments to evaluate treatment durability, long-term outcomes, and potential late effects. Monitor participants for any delayed adverse events or treatment-related complications. Maintain ongoing communication with trial participants and stakeholders to ensure transparency and accountability.

Regulatory Submission and Approval: Prepare regulatory submissions for marketing authorization or approval based on the trial results. Collaborate with regulatory authorities to facilitate the review and approval process. Obtain regulatory approval for new treatments or indications based on the trial findings.

Post-trial Surveillance and Pharmacovigilance: Implement post-marketing surveillance and pharmacovigilance activities to monitor the safety and effectiveness of approved treatments in real-world settings. Collect and analyze post-market data to identify rare or long-term adverse events and inform risk management strategies.

By following these steps and adhering to rigorous scientific and ethical standards, researchers can effectively conduct platform trials to evaluate multiple treatments and advance medical knowledge for the benefit of patients and healthcare systems

Future

The future of platform trials appears promising, with ongoing advancements and increasing adoption across various fields of medical research. Several factors contribute to the growing significance and potential of platform trials:

Efficiency and Cost-Effectiveness: Platform trials offer a more efficient and cost-effective approach to evaluating multiple treatments simultaneously. By sharing infrastructure, resources, and data across multiple treatment arms, these trials can expedite the drug development process, potentially reducing costs and timelines.

Adaptive Design: The adaptive design of platform trials allows for flexibility in incorporating new treatments, modifying trial protocols based on emerging data, and dropping ineffective treatments. This adaptive nature enhances the likelihood of identifying successful treatments and optimizing patient outcomes.

Precision Medicine and Personalized Treatments: Platform trials enable the evaluation of treatments tailored to specific patient populations or disease subtypes, facilitating the advancement of precision medicine approaches. By analyzing data from diverse patient groups, researchers can identify biomarkers and predictive factors to guide personalized treatment decisions.

Collaborative Research Networks: Platform trials often involve collaboration among multiple institutions, research organizations, pharmaceutical companies, and regulatory agencies. These collaborative networks foster interdisciplinary cooperation, data sharing, and knowledge exchange, accelerating scientific discoveries and the translation of research findings into clinical practice.

Expansion to Diverse Disease Areas: While platform trials have gained prominence in fields such as oncology and infectious diseases, their applicability extends to a wide range of disease areas, including neurology, cardiology, rare diseases, and beyond. As researchers continue to explore new therapeutic targets and treatment modalities, platform trials offer a versatile framework for evaluating innovative therapies across diverse patient populations.

Digital Health Technologies: The integration of digital health technologies, such as wearable devices, remote monitoring tools, and electronic health records, enhances the data collection and monitoring capabilities of platform trials. These technologies enable real-time data capture, remote patient monitoring, and decentralized trial conduct, making trials more patient-centric and adaptable to evolving healthcare needs.

Regulatory Support and Guidelines: Regulatory agencies, including the FDA and EMA, have shown increasing interest in platform trials and have provided guidance to support their implementation. Clear regulatory pathways and frameworks facilitate the design, conduct, and approval of platform trials, encouraging their adoption in drug development and regulatory decision-making.

Overall, the future of platform trials holds promise for revolutionizing clinical research, advancing therapeutic innovation, and improving patient outcomes across diverse disease areas. Continued investment in collaborative research initiatives, technological innovation, and regulatory support will be essential in realizing the full potential of platform trials in shaping the future of medicine.

Platform trials have become increasingly common, and evidence is needed to determine how this trial

design is actually applied in current research practice.

Objective: To determine the characteristics, progression, and output of randomized platform trials.

Evidence review: In this systematic review of randomized platform trials, Medline, Embase, Scopus, trial registries, gray literature, and preprint servers were searched, and citation tracking was performed in July 2022. Investigators were contacted in February 2023 to confirm data accuracy and to provide updated information on the status of platform trial arms. Randomized platform trials were eligible if they explicitly planned to add or drop arms. Data were extracted in duplicate from protocols, publications, websites, and registry entries. For each platform trial, design features such as the use of a common control arm, use of nonconcurrent control data, statistical framework, adjustment for multiplicity, and use of additional adaptive design features were collected. The progression and output of each platform trial were determined by the recruitment status of individual arms, the number of arms added or dropped, and the availability of results for each intervention arm.

Findings: The search identified 127 randomized platform trials with a total of 823 arms; most trials were conducted in the field of oncology (57 [44.9%]) and COVID-19 (45 [35.4%]). After a more than twofold increase in the initiation of new platform trials at the beginning of the COVID-19 pandemic, the number of platform trials has since declined. Platform trial features were often not reported (not reported: nonconcurrent control, 61 of 127 [48.0%]; multiplicity adjustment for arms, 98 of 127 [77.2%]; statistical framework, 37 of 127 [29.1%]). Adaptive design features were only used by half the studies (63 of 127 [49.6%]). Results were available for 65.2% of closed arms (230 of 353). Premature closure of platform trial arms due to recruitment problems was infrequent (5 of 353 [1.4%]).

Conclusions and Relevance: This systematic review found that platform trials were initiated most frequently during the COVID-19 pandemic and declined thereafter. The reporting of platform features and the availability of results were insufficient. Premature arm closure for poor recruitment was rare [1]

[1]

Griessbach A, Schönenberger CM, Taji Heravi A, Gloy V, Agarwal A, Hallenberger TJ, Schandelmaier S, Janiaud P, Amstutz A, Covino M, Mall D, Speich B, Briel M. Characteristics, Progression, and Output of Randomized Platform Trials: A Systematic Review. JAMA Netw Open. 2024 Mar 4;7(3):e243109. doi: 10.1001/jamanetworkopen.2024.3109. PMID: 38506807.